PAEDIATRIC ENDOCRINOLOGY

	T1DM	DKA	ADDISON (adrenal insufficiency)
PP	Autoimmune destruction of pancreatic B cells leading to insulin deficiency ➢ 25-50% of new T1DM present in DKA	Insulin deficiency – unable to utilise glucose switching to anaerobic metabolism and fatty acid oxidation for ketones	Adrenal glands do not produce sufficient steroid hormones (esp. cortisol and aldosterone) **Primary**: **Autoimmune Addison** (most common **Secondary**: **inadequate ACTH** secondary to congenital hypoplasia of pituitary **Tertiary**: **inadequate CRH release** due to long-term steroid usage > 3 wks → sudden withdrawal of steroids means endogenous steroids not produced
RF	• FHx of autoimmune diseases • Genetics • Viral trigger – Coxsackie B and enterovirus	• T1DM • Infection	➢ FHx of autoimmune disease ➢ Long-term steroid usage (tertiary)
Sx	• Polyuria • Polydipsia • FTT - UWL (due to severe dehydration) • Secondary enuresis (bedwetting in previously dry child)	• Polyuria + polydipsia → UWL • N/V + abdo pain • Kussmaul's breathing • Sweet smelling acetone breath • Syncope – altered LOC	**Babies + Children** ➢ *Lethargy, vomiting,* ➢ *FTT - poor feeding, poor wt gain* ➢ *Hypoglycaemia* ➢ *Jaundice* **Children specific** ➢ Abdo pain ➢ Muscle weakness and cramps ➢ **Bronze hyperpigmentation** (*elevated ACTH and MSH stimulate melanocytes)* ➢ **Developmental delay + poor academic performance**
Comp.	➢ **Short-term** ○ **Hyperglycemia** (DKA) ○ **Hypoglycemia** (*XS exogenous insulin*) – SA +LA CHO → IV 10% dextrose 2mg/kg bolus or IM glucagon ○ **Nocturnal Hypoglycaemia –** sweaty child overnight → alter insulin regime ➢ **Long-term** – monitor **microvascular** (eye, neuro, nephron) and **macrovascular** complications. (PVD, IHD, CAD, Stroke, HTN)	➢ **Ketoacidosis** ➢ **Severe dehydration** ➢ **Hyperkalaemia** - arrythmias ➢ **Cerebral oedema** (rapid IV bolus) – headache, altered behaviour, bradycardia ○ **Slow IV fluids** ○ **Mannitol** ○ **IV 3% hypertonic saline**	**Addisonian (adrenal) crisis** ➢ HyperK ➢ HypoNa ➢ Hypoglycemia ➢ HypoTN
Ix	➢ FBC, EUC ➢ BSL ➢ Blood cultures (if fever present) ***Autoimmune screen*** ➢ C-peptide, proinsulin ➢ Anti-GAD, Zn8 transporter, Islet cell antibodies ➢ TFT - anti-TPO (autoimmune) ➢ Anti-TTG - coeliac	• **EUC**- hyperkalaemia • **BSL** – high > 11mM • **ABG** – metabolic acidosis – pH < 7.3 • **Blood ketones** > 3mM • **Urine dipstick** - ketones	• **FBC** • **EUC** – check potassium • **BSL** • **Aldosterone : renin ratio** • **Short-synacthen test** (measure blood cortisol at baseline, 30 and 60 mins) ○ Failure of cortisol to rise (> 2x baseline) = Addison • **Cortisol + ACTH** levels (measure before steroid administration) Addison: Cortisol Low, ACTH High, Aldo Low, Renin High 2nd: Cortisol Low, ACTH Low, Aldo Normal, Renin Normal
Mx	➢ **MDT approach** – **education + reassurance** – paediatric endocrinologist, diabetic nurse educator, paediatrician, dietician, ophthalmologist, podiatrist ➢ **Insulin dependent**: (titrate accordingly) ○ SA – Actrapid ○ LA – lantus ○ Insulin pump (dexcom) ➢ **Monitor CHO intake** ➢ **Monitor BSL control** ○ HbA1C (every 3-6/12) ○ Freestyle Libre (PBS)	➢ Refer to paediatricians → ABCD ➢ *IV access* ○ **IVF – 0.9% NS infusion over 48 hrs** (NOT bolus) to avoid cerebral oedema ○ **IV insulin fixed rate** ○ **IV dextrose** if BSL < 14mM (prevent relative) hypoglycaemia) ○ **IV K+** (if hypokalemia) ➢ *Treat underlying cause* ○ ABx for sepsis ○ 3% hypertonic saline for cerebral oedema	***Acute Mx of Addisonian crisis:*** ➢ *ICU monitoring* ➢ *IV hydrocortisone* ➢ *IVF* ➢ *Correct hypoBSL → IV 10% dextrose* ➢ *Monitor and correct fluid and electrolyte* ***Replacement steroids***: ➢ Fludrocortisone – mineralocorticoid (for aldo) ➢ Hydrocortisone - glucocorticoid (for cortisol) ***Long-term*** ➢ ID tag – steroid card ➢ Educate "**sick day rules**" – increase steroid dosage during acute illnesses to match normal steroid response ➢ Paediatric endocrinologist – monitor ○ Growth and development ○ BP ○ EUC ○ BSL ○ Bone profile ○ Vitamin D

Other causes of hypoglycaemia

- Hypothyroidism
- Glycogen storage disorder
- GH deficiency
- Liver cirrhosis
- Alcohol
- Fatty acid oxidation defects (e.g. MCADD)

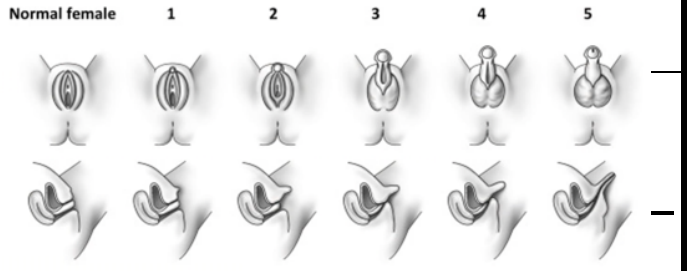
	Congenital adrenal hyperplasia (CAH)	Growth hormone def.	Hypothyroidism
PP	Congenital deficiency of 21-OH enzyme – mainly (**autosomal recessive pattern**) **XS progesterone is shunted towards androgen synthesis pathway in adrenal gland** ➢ Under-production → cortisol and aldo ➢ Over-production → androgens **Primary adrenal insufficiency (peripheral):** ➢ 73% CAH ➢ 13% acquired (autoimmune failure or adrenal haemorrhage) **Secondary adrenal insufficiency (central):** ➢ Pituitary dysfn ➢ Hypothalamic dysnf (tertiary adrenal insufficiency) *Assoc w/ hypothyroidism and GH def. and DI (if post. pituitary affected)	Deficiency in growth hormone released by pituitary gland due to: ➢ **Genetic mutation** (GH1 o GHRHR genes) ➢ **Empty sella syndrome** (under-developed or damaged pituitary gland) ➢ **Acquired** – secondary to infection, trauma or post-op	**Congenital** - 1 in 3000 born w/ underactive thyroid (dysgenesis) or dysfunctional thyroid gland (dyshormogenesis) **Acquired** ➢ **Normal thyroid becomes underactive** ➢ **Usu. in child or adolescent**
RF	➢ Consanguineous parents – increases risk of double mutants		➢ FHx of thyroid disease ➢ FHx of autoimmune disease
Sx	**Males** ➢ **Tall for age** ➢ **Deep voice** ➢ **Early puberty** ➢ Large penis ➢ Small testes **Females** ➢ **Tall for age** ➢ **Deep voice** ➢ **Early puberty** ➢ Virilised or ambiguous genitalia ➢ Facial hair (hirsutism) ➢ Skin hyperpigment	**Neonates:** • **Micropenis** • Hypoglycemia • **Severe jaundice** **Infants and children** • FTT – short stature, poor wt gain • Slow development of movement and strength • Delayed puberty	➢ **Prolonged jaundice (> 72 hrs after birth)** ➢ **FTT – poor feeding** ➢ **Constipation** ➢ **Sleepy** ➢ **Fatigue or low energy** ➢ **Dry skin and hair loss** ➢ **Weight gain**
Comp.	**Severe CAH – similar to Addisonian crisis** ➢ **Hyperkalemia** ➢ **hypoNa** → polydipsia, dehydration signs ➢ **hypoglyceamia** - *confused, air hunger, diaphoresis, palp.* ➢ **hypoTN** – light-headed, N/V	➢ Reduced QoL ➢ May present with other deficiencies: o Hypogonadism (LH/FSH) o Adrenal insufficiency o Hypothyroidism o Hypopituitarism	➢ Myxodema coma – Hashimoto's thyroiditis
Ix	➢ **Newborn screening (check for ↑↑17-OH progesterone)** ➢ **Low 24-hr cortisol - Adrenal insufficiency (short synacthen test – ACTH stimulation)** ➢ **Low aldo** = salt wasting + HypoTN ➢ **High Androgen** (high TT/DHEA) = masculinisation ➢ Genetic testing 1) **Classical salt wasting** = **early presentation 7-14 days,** FTT, dehydrated with hypoNa, hyperK, hypoBSL 2) **NON-classical salt-wasting** = **later presentation 2-4yo** with virilisation, growth spurt etc.	• **GH stimulation test** (e.g. glucagon, insulin, arginine and clonidine) → poor response if deficiency • **OGTT – elevated BSL** • **IGF-1 assay - low** • **MRI brain** + hypothalamus • **Genetic test** – Prader-willi syndrome and Turner's syndrome • **XR (L wrist) or DEXA scan** – to determine bone age → helps predict final height	• Newborn blood spot test • TFT • Anti-TPO, Anti-TSHR, Anti-Tg • Thyroid neck USS
Mx	**Refer to specialist paediatric endocrinologists** Rx with stress steroids ➢ IV Fludrocortisone – mineralocorticoid (for aldo) ➢ IV Hydrocortisone STAT 25mg-100mg- glucocorticoid (for cortisol ➢ IVF 0.9% NS replacement and maintenance ➢ Corrective surgery – ambiguous genitalia in girls	**Refer to specialist paediatric endocrinologists** ➢ Daily SC GH injections (e.g. somatotropin) ➢ Closely monitor height and development	**specialist paediatric endocrinologists** ➢ Levothyroxine once daily PO ➢ Titrate dosage and monitor TFTs closely

Disorders of sexual development (DSD) + (intersex)

	46 XX DSD,	46 XY DSD	Sex chr. DSD
PP	**androgen XS** ➢ **CAH** (90% in 21-OH enzyme def.) → cannot convert PG into cortisol (XS androgen) ➢ **Aromatase def.** ➢ **iatrogenic**	**androgen synthesis def.** ➢ gonadal dysgenesis (Swyer syndrome) ➢ gonadal regressions ➢ androgen synthesis defect (defective SRY gene) ➢ AIS ➢ Persistent Mullerian duct syndrome	➢ **45XO turner** – webbed neck, short, wide carrying angle, mental retard, infertile ➢ **47XXY Klinefelter** – tall, thin, small testes, gynecomastia , infertile ➢ **Chimerism** ➢ **Mixed gonadal dysgenesis**
Sx	**Male characteristic in female** (e.g. virilisation, muscle bulk, clitoromegaly)	**Female phenotype but male genotype** (NO TT or AMH → looks female)	
Ix	**CAH: (AR defect – 21-OH def.)** ➢ Low cortisol ➢ Low aldo = salt wasting + HypoTN ➢ High Androgen = masculinisation	**AIS (X-linked recessive)** ➢ Female phenotype ➢ Unresponsive to male androgen but responsive to estrogen	Karyotyping

Prader Staging:
0 = *normal genitalia*
1 = *clitoromegaly*
2 = *clearly abnormal clitoromegaly*
3 = obvious small penis

Prader Staging:



MDT involved:
- **Endocrinologist, GP, Surgeon (paediatric urologist, gynaecologists)**
- **Psychologists**
- **Social workers**
- **Family**

Active discussions:
- **Gender assignment (psychosocial, fertility potential, HRT?)**
- **?Surgical correction (*informed decision making*)**